AMENDMENTS TO THE CLAIMS

This listing replaces all prior versions and listings of claims in the application.

Listing of Claims

1. (Previously Presented) A method for determining the type of biocompatible polymer, the extent of modification, and the conditions for modification of a therapeutic agent with a biocompatible polymer to prevent host-mediated inactivation of said therapeutic agent when covalently modified by said biocompatible polymer, comprising:

(a) assaying a biological activity of a first modified therapeutic agent after said first modified therapeutic agent has been administered to a subject, wherein said first modified therapeutic agent is covalently modified with a biocompatible polymer;

(b) assaying the biological activity of said first modified therapeutic agent after at least one booster dose of said first modified therapeutic agent has been administered to said subject;

(c) assaying the biological activity of a second modified therapeutic agent after said second modified therapeutic agent has been administered to a subject, wherein said second modified therapeutic agent is covalently modified with a biocompatible polymer and wherein at least one condition selected from the group consisting of the type of biocompatible polymer, the extent of modification, and the conditions for modification differs from the conditions of said first modified therapeutic agent;

(d) assaying the biological activity of said second modified therapeutic agent after at least one booster dose of said second modified therapeutic agent has been administered to said subject; and

(e) comparing the biological activity of said first modified therapeutic agent with the biological activity of said second modified therapeutic agent to select the type of biocompatible polymer, the extent of modification, and the conditions for modification that prevent host-mediated inactivation of said therapeutic agent when covalently modified by said biocompatible polymer.

2. (Previously Presented) The method of claim 1, wherein said second modified therapeutic agent is modified with the same biocompatible polymer as said first modified therapeutic agent.

3. (Previously Presented) The method of claim 2, wherein said biocompatible polymer is polyethylene glycol (PEG).

4. (Original) The method of claim 3, wherein said PEG is selected from the group consisting of mono-methoxy succinimidyl butanoate (SBA)-PEG, succinimidyl carbonate (SC)-PEG, aldehyde (ALD)-PEG, and succinimidyl propionate (SPA)-PEG.

5. (Previously Presented) The method of claim 1, wherein said second modified therapeutic agent is modified to the same extent as said first modified therapeutic agent.

6. (Previously Presented) The method of claim 1, wherein said second modified therapeutic agent and said first modified therapeutic agent are modified with different biocompatible polymers.

7. (Previously Presented) The method of claim 1, wherein said therapeutic agent comprises a polypeptide.

8. (Original) The method of claim 7, wherein said polypeptide is used to treat viral infections in patients in need of treatment thereof.

9. (Original) The method of claim 7, wherein said polypeptide is used to treat cancer in patients in need of treatment thereof.

10. (Original) The method of claim 7, wherein said polypeptide has a monomeric molecular weight of about 300 daltons to about 300,000 daltons.

11. (Original) The method of claim 7, wherein said polypeptide is used to lower glutamine levels in a subject.

12. (Original) The method of claim 7, wherein said polypeptide is used to lower asparagine levels in a subject.

13. (Original) The method of claim 7, wherein said polypeptide is used to lower asparagine and glutamine levels in a subject.

14. (Previously Presented) The method of claim 1, wherein said therapeutic agent is a nucleic acid.

15. (Previously Presented) The method of claim 14, wherein said nucleic acid is used to treat a viral infection in patients in need of treatment thereof.

16. (Previously Presented) The method of claim 14, wherein said nucleic acid is used to treat cancer in patients in need of treatment thereof.

17. (Previously Presented) A method of preparing a pharmaceutical composition where host-mediated inactivation is prevented, comprising selecting the type of biocompatible polymer, the extent of modification, and the conditions for modification of a therapeutic agent by the method of claim 1 and modifying said therapeutic agent according to the type of biocompatible polymer, the extent of modification, and the conditions for modification selected.

18. (Original) The method of claim 17, wherein said pharmaceutical composition further comprises an excipient.

19. (Original) The method of claim 18, wherein said excipient protects said therapeutic agent during lyophilization.

20. (Original) The method of claim 17, wherein said therapeutic agent comprises glutaminase-asparaginase.

21. (Previously Presented) The method of claim 20, wherein said therapeutic agent comprises *Pseudomonas* glutaminase-asparaginase.

22. (Original) The method of claim 21, wherein said *Pseudomonas* glutaminase-asparaginase is modified with polyethylene glycol.

23. - 40. (Cancelled)

41. (Previously Presented) The method of claim 1, wherein the subject administered the first modified therapeutic agent is different from the subject administered the second modified therapeutic agent.

42. (Previously Presented) A method for determining the type of biocompatible polymer, the extent of modification, and the conditions for modification of a therapeutic agent with a biocompatible polymer to prevent host-mediated inactivation of said therapeutic agent when covalently modified by said biocompatible polymer, comprising:

(a) selecting a biological activity;

(b) assaying the selected biological activity of step (a) of a first modified therapeutic agent after said first modified therapeutic agent has been administered to a subject, wherein said first modified therapeutic agent is covalently modified with a biocompatible polymer;

(c) assaying the selected biological activity of step (a) of said first modified therapeutic agent after at least one booster dose of said first modified therapeutic agent has been administered to said subject;

(d) assaying the selected biological activity of step (a) of a second modified therapeutic agent after said second modified therapeutic agent has been administered to a subject, wherein said second modified therapeutic agent is covalently modified with a biocompatible polymer and wherein at least one condition selected from the group consisting of the type of biocompatible polymer, the extent of modification, and the conditions for modification differs from the conditions of said first modified therapeutic agent;

(e) assaying the selected biological activity of step (a) of said second modified therapeutic agent after at least one booster dose of said second modified therapeutic agent has been administered to said subject; and

(f) comparing the selected biological activity of step (a) of said first modified therapeutic agent with the selected biological activity of step (a) of said second modified therapeutic agent to select the type of biocompatible polymer, the extent of modification, and the conditions for modification that prevent host-mediated inactivation of said therapeutic agent when covalently modified by said biocompatible polymer.

43. (Previously Presented) A method according to claim 42, wherein the step of selecting a biological activity comprises selecting a biological activity other than either antigenicity or immunogenicity.

44. (Previously Presented) A method for determining the type of biocompatible polymer, the extent of modification, and the conditions for modification of a therapeutic agent with a biocompatible polymer to prevent host-mediated inactivation of said therapeutic agent when covalently modified by said biocompatible polymer, comprising:

(a) selecting a biological activity;

(b) assaying the selected biological activity of step (a) of a first modified therapeutic agent after said first modified therapeutic agent has been administered to a subject, wherein said first modified therapeutic agent is covalently modified with a biocompatible polymer;

(c) assaying the selected biological activity of step (a) of said first modified therapeutic agent after at least one booster dose of said first modified therapeutic agent has been administered to said subject;

(d) assaying the selected biological activity of step (a) of a second modified therapeutic agent after said second modified therapeutic agent has been administered to a subject, wherein said second modified therapeutic agent is covalently modified with a biocompatible polymer and wherein at least one condition selected from the group consisting of the type of biocompatible polymer, the extent of modification, and the conditions for modification differs from the conditions of said first modified therapeutic agent;

(e) assaying the selected biological activity of step (a) of said second modified therapeutic agent after at least one booster dose of said second modified therapeutic agent has been administered to said subject; and

(f) comparing the selected biological activity of step (a) of said first modified therapeutic agent with the selected biological activity of step (a) of said second modified therapeutic agent to determine the relative bioavailability of said first modified therapeutic agent and said second therapeutic agent (g) selecting the type of biocompatible polymer, the extent of modification, and the conditions for modification that prevent host-mediated inactivation of said therapeutic agent when covalently modified by said biocompatible polymer based upon the comparison of step (f).

45. (Previously Presented) A method according to claim 44, wherein the step of selecting a biological activity comprises selecting a biological activity other than either antigenicity or immunogenicity.

46. (Previously Presented) A method according to claim 1, wherein the step of selecting a biological activity comprises selecting a biological activity other than either antigenicity or immunogenicity.